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Supportive Care: Comprehensive conservative care in end-stage kidney disease

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Keywords:	patient-centered care, chronic kidney disease, conservative care, palliative care, supportive care, quality of life
Abstract:	<p>Conservative (non-dialytic) kidney care is widely recognized and delivered, but until recently has not been clearly defined. This paper provides a clear definition of comprehensive conservative care, as holistic patient-centered care for patients with end-stage chronic kidney disease. This includes interventions to delay progression of kidney disease and minimize complications, as well as detailed communication, shared decision making, advance care planning, psychological and family support. It does not include dialysis.</p> <p>Limited epidemiological evidence from Australia and Canada indicates that for every new person diagnosed with end-stage kidney disease who receives dialysis or transplant, there is one new person that is managed conservatively (either actively or not). For older patients (those over 75 or 80 years) who have higher levels of co-morbidity (such as diabetes, heart disease) and poorer functional status, the survival advantage of dialysis may be limited, and comprehensive conservative management should be considered. Robust comparative evidence remains limited however.</p> <p>As well as survival, considerations of symptoms, quality of life, and hospital-free days are important for patients and families, and there is some evidence that communication about possible conservative management options is generally insufficient, even where comprehensive conservative care pathways are already established.</p> <p>There is almost no evidence about which models of care and which interventions might be most beneficial in this population; symptom control and the cost-effectiveness of interventions are addressed in the companion papers within this series.</p>

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Comprehensive Conservative Care in End-Stage Kidney Disease

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Abstract

Conservative (non-dialytic) kidney care is widely recognized and delivered, but until recently has not been clearly defined. This paper provides a clear definition of comprehensive conservative care, as holistic patient-centered care for patients with end-stage kidney disease. This includes interventions to delay progression of kidney disease and minimize complications, as well as detailed communication, shared decision making, advance care planning, psychological and family support. It does not include dialysis.

Limited epidemiological evidence from Australia and Canada indicates that for every new person diagnosed with end-stage kidney disease who receives dialysis or transplant, there is one new person that is managed conservatively (either actively or not). For older patients (those over 75 or 80 years) who have higher levels of co-morbidity (such as diabetes, heart disease) and poorer functional status, the survival advantage of dialysis may be limited, and comprehensive conservative management should be considered. Robust comparative evidence remains limited however.

As well as survival, considerations of symptoms, quality of life, and hospital-free days are important for patients and families, and there is some evidence that communication about possible conservative management options is generally insufficient, even where comprehensive conservative care pathways are already established.

There is almost no evidence about which models of care and which interventions might be most beneficial in this population; symptom control and the cost-effectiveness of interventions are addressed in the companion papers within this series.

Defining conservative care

Conservative (non-dialytic) kidney care is widely recognized and delivered, but until recently has not been clearly defined. A range of different terms, such as conservative care, maximal conservative management, palliative care, and supportive care, have been used in relation to non-dialysis care in end-stage kidney disease, but without clear definition. This has constrained recognition of the health-care needs of this sector of the end-stage kidney disease population, and has prevented systematic study to build evidence on ways to best improve care and outcomes.

Box 1: Definition of comprehensive conservative care

'Comprehensive conservative care' is planned holistic patient-centred care for patients with Stage 5 (glomerular filtration rate category 5) Chronic Kidney Disease that includes:

- Interventions to delay progression of kidney disease and minimize risk of adverse events or complications
- Shared decision making
- Active symptom management
- Detailed communication, including advance care planning
- Psychological support
- Social and family support
- Cultural and spiritual domains of care

Comprehensive conservative care does not include dialysis.

From the Kidney Disease | Improving Global Outcomes (KDIGO) Controversies Conference on Supportive Care in Chronic Kidney Disease (1)

To counter this, a recent consensus conference (1) proposed a detailed, specific definition for conservative care in end-stage kidney disease, suggesting adoption of the term 'comprehensive conservative care' to reflect the full extent of conservative management, and providing a full definition (see Box 1) of what comprehensive conservative care should include. The conference also proposed three distinct groups within the conservative care population (see Box 2), to address concerns about availability of renal replacement therapy and options for choice across the spectrum of low-, middle-, and high-income countries.

Box 2: Distinct conservative care populations

1. Comprehensive conservative care. Conservative care that is chosen or medically advised.
2. Choice-restricted conservative care. Conservative care for patients in whom resource constraints prevent or limit access to renal replacement therapy; therefore, a choice for conservative care cannot be recognized.
3. Unrecognized Stage 5 (glomerular filtration rate category 5) chronic kidney disease. Chronic kidney disease is present but has not been recognized or diagnosed; therefore, a choice for conservative care cannot be recognized.

From the Kidney Disease | Improving Global Outcomes (KDIGO) Controversies Conference on Supportive Care in Chronic Kidney Disease (1)

How common is conservative care?

One of the first considerations is understanding the size of the population of those with end-stage kidney disease who are managed conservatively. There is very limited evidence on the incidence or prevalence of conservative care of end-stage kidney disease, and population-based needs assessments in relation to conservative care are rare. In 2011, a detailed whole population-based study was published in Australia to estimate the total incidence of end-stage kidney disease (2), including (for the first time) both those treated with renal replacement therapy and those receiving conservative care. Previous evidence on end-stage kidney disease from the national and international Renal Registries has been limited to those with dialysis or transplant. The authors identified 21,500 new cases of end-stage kidney disease in Australia during the period 2003 – 2007 (2); this amounted to 21 cases per 100,000 people (20.9 per 100,000 population, with 95% confidence intervals of 18.3 – 24.0 per 100,000 population). For every new case who received dialysis or transplant, there was about one new case that did not.

A recent community-based cohort study in Canada demonstrated that, during median follow-up of 4.4 years of 1,816,824 adults with measured eGFR in Alberta, Canada, 5.36% died, with 0.18% who developed kidney failure that was treated and 0.17% who developed kidney failure that was managed conservatively (3). As in the Australian population based study (1), for every new case who received dialysis or transplant, there was about one new case that did not, and rates of untreated kidney failure were consistently higher at older ages. Both studies indicate that the incidence of advanced kidney disease in older people may be higher than previously thought, and certainly there are greater than expected rates of untreated kidney failure among the oldest patients. It may be that further population-based studies in other countries would show similarly higher than expected levels of conservative management of end-stage kidney disease.

In interpreting these findings, there are some major limitations. First, national data is only as yet available from Australia and Canada, and may not apply to other countries and contexts. Secondly, just as dialysis patterns have changed over time, so it is probable that patterns of conservative care have changed over time. It is worth noting that in the Australian whole population-based study, neither the overall proportion of new cases managed with conservative care nor the age standardized rate of conservative care consistently changed over time period 2003 – 2007, but this is a relatively short timeframe, and further study across more extended time periods is needed. Thirdly, and perhaps most important of all, this data relates only to high income countries; the limited availability of dialysis in some low- and middle-income countries may have a profound impact on the apparent prevalence of 'conservative management', and underlines the importance of defining and understanding the different sectors of the population who are managed without dialysis (as defined in Box 2).

What is the evidence on survival in conservative care?

A further consideration is survival of those managed without dialysis. One of the main challenges in studying and comparing survival between dialysis and conservative populations is the bias inherent in the pathway decision. Those who are more fit usually opt for dialysis, and many choose or are advised to have conservative management because of co-morbidity or other factors which in themselves adversely influence survival. Without randomization into either group, it is difficult to attribute survival differences to either dialysis or conservative management. In addition, many studies do not compare survival, hospital days and symptoms, or quality of life between the two populations; any meaningful comparison needs to consider not only survival, but also the nature of any additional days of survival. Days spent attending or in hospital, or with poor quality of life are not rated as highly by patients as hospital-free days, and days with good quality of life (4).

The key evidence on survival of patients managed conservatively can be distilled from fourteen studies (5) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18). These are excellently summarized in the systematic review by O'Connor (19), with later studies by Silva Gane et al (15) and Hussain (18). In the absence of randomized controlled trials (ethically and practically difficult, if not impossible), each of these studies is flawed in one way or another. Only about half (6) (7) (10) (11) (13) (14) (15) (18) compare survival between conservative patients and those on dialysis. The main flaws relate to significant differences in the comparison groups with regard to age profiles, how conservative/dialysis decisions were made, varying time from which survival is measured (including computing or assuming actual or putative 'dialysis start' dates), likely changes in referral and dialysis practices over recent decades, and the reality that it is only truly legitimate to compare survival outcomes when each group is eligible for both treatment options (20). Some studies provide further context for the end-stage kidney disease and report co-morbidity or level of dependence/performance but scoring systems vary and the Charlson score in particular may "double count" or over-score age. In contrast, frailty - which is very common in this population and independently associated with increased mortality - is rarely measured or reported.

An additional challenge is that the conservative care population is heterogeneous. It includes at least three groups of patients whose survival is likely to be very different; first, those suitable for dialysis who choose not to receive it, second, older people with high co-morbidity where dialysis is not offered, and third, patients who lack capacity and may not always be offered dialysis. Although some of the studies try to make these distinctions, the numbers in the conservative management arms are often small and difficult to analyze with precision. In France, a multicenter prospective cohort study of 581 older patients (mean age 82 years) with end-stage kidney disease has shown that, despite a high prevalence of comorbidities, most patients are autonomous and living at home. At inclusion, 43% postponed the dialysis decision due to stable estimated glomerular filtration rate, 17% were under evaluation, 24% chose dialysis, and 16% decided not to have dialysis (21). Szeto et al present data on 25 patients who were considered suitable for but declined dialysis; and

contrasted this group with 38 patients who were not considered suitable for dialysis, mainly because of multiple co-existing medical illnesses. The former 'declining group' were younger and less co-morbid than the latter group, and yet had no difference in survival (17). Another confounder is that most studies do not address survival advantage/excess mortality of patients, in relation to life expectancy of age-matched period-specific individuals in the general population.

Among the key survival studies, the work by Joly studying those 80 years and over (6) is notable for long follow up (up to 12 years) so that differences in referral patterns could be sought over different time periods. Those not put forward for dialysis were of similar age but were more likely to be socially isolated, referred later, diabetic, and have poorer performance. Survival was significantly longer in the dialyzed group (28.9 versus 8.9 months). Usefully, the 2.4 year life expectancy of the dialyzed octogenarians was related to population norms, and represented about one quarter to one third of the life expectancy of the general population over 80 years as reported in national life expectancy statistics in France at the time. In contrast, the most widely cited paper of Smith et al (7) is based on very small numbers (10 and 26 respectively), comparing those recommended not to dialyze who nevertheless decided to dialyze, and those who followed the recommended conservative pathway. Their finding of no significant survival advantage (8.3 months versus 6.3 months) between these frail elderly patients was important despite the small numbers, and despite the fact that a putative dialysis initiation date was based on eGFR of <10 ml/min estimated using the Cockcroft-Gault formula. In this study, 65% of the deaths occurring in the dialyzed patients took place in hospital compared with 27% in the conservative group (used as a surrogate quality indicator).

Carson (13) attempted to "start the clock" at an equivalent time in the comparative groups (all incident patients 70 years and older) by computing 'putative' dialysis start times (e-GFR 10.8ml/min/m²) which mirrored practice in the dialysis group (13). They showed significant survival advantage in the dialyzed group (37.8 versus 13.9 months), but the conservative group were approximately 10 years older; statistical corrections could not be made to correct for this age difference because of the small numbers. The conservative patients were more likely to die at home or in a hospice (again, used as an indirect quality marker) and the authors computed that every day of additional survival was almost at the expense of a day spent either as an inpatient or attending hospital for dialysis (hospitalization 0.069 versus 0.043 hospital days per patient days survived) (13). A different approach was adopted by Murtagh et al, who measured survival from estimated GFR < 15 mL/min (10). They confined their analysis to all those with Stage 5 chronic kidney disease over 75 years known to nephrology clinic. Once again, the overall survival was better in the dialysis group but this advantage was lost in patients with high comorbidity. There are a number of caveats to this study. No 'late presenters' were included (so this may not reflect real life practice and cannot be compared with studies where all incident patients are included). The age of the conservative group was 4 years older than the dialysis group, and perhaps most importantly, the analysis was on an 'intention to treat' basis. 24 patients (24/52) who

chose the dialysis pathway did not actually receive dialysis by the study end either because they died (n= 8) or because dialysis had not yet started (n= 16).

Szeto reported on survival of 63 conservative patients, and while these authors did not attempt to compare conservative and dialysis groups, they do (like Carson et al) provide useful data on the sub-group who declined dialysis (n= 25) (17). These were on average a decade younger and had much lower co-morbidity scores but – importantly - their survival was not significantly different from the conservative group. The median survival from the date of needing dialysis (7mls/min) was 6.58 months. Of note also only 36/63 were deemed to have died from uraemia, with other unrelated deaths occurring both before (n= 12) and after the theoretical date of needing dialysis (n=7). Taking this study and inferring from other studies (6) (7) (13), there is fair evidence that the median survival from e-GFR 6-7 ml/min is around 6 months.

The more recent papers (14) (18) offer the best available evidence on survival. Work by Chandna and colleagues spans an 18 year period and involving 844 patients, 155 (18%) of whom received conservative care (14). Conservative patients were older and had higher co-morbidity. Again there was an overall survival advantage to dialysis (mean survival 21.2 versus 67.1 months $p<0.001$). However (as earlier studies had indicated, but less robustly), for patients over 75 years the survival advantage of dialysis reduced to only 4 months (non-significant) when corrected for age, high co-morbidity and diabetes. Similarly, in a retrospective observational study of patients over the age of 70 years attending pre-dialysis clinic comparative survival, Hussain reported hospital admission and palliative care access outcomes between patients managed conservatively or choosing renal replacement therapy (18). Survival, measured from three time points for both groups (e-GFR was $<20\text{mL/min}$, $<15\text{ mL/min}$ and $<12\text{ mL/min}$), showed that dialysis conferred a significant survival advantage. However, there was a significant reduction in the effect of dialysis pathway on survival for those with high Charlson comorbidity index. Hospital admissions were greater and chances of dying at home were less in the dialysis patients. There was no survival advantage from dialysis in the >80 year olds with high co-morbidity or poor functional status at all levels of disease severity.

What about symptoms, quality of life and illness experience in conservative care?

It is not only survival that is important, but crucially the symptoms, quality of life and experience of illness on the conservative management pathway. Once again there is limited evidence. O'Connor's systematic review provides the best summary of evidence about symptoms and quality of life (19). Six studies describe symptom burden and/or quality of life. Most are cross sectional in design and all received a level 2 - or intermediate - strength of recommendation taxonomy rating in the review (19) (22). Three studies used the Memorial Symptom Assessment Schedule to collect data (23) (24) (25), while one study used a modified POSs (26). Three articles directly measured quality of life (11) (25) (27), using standardized tools. One study also used interviews (11) .

All report significant symptom burden in those undergoing conservative care, with numbers of symptoms varying from 6.8 to 17 per individual patient. These studies were remarkably consistent in terms of reporting similar symptoms and similar patterns of prevalence. Where reported, there was a considerable increase in symptoms in the month prior to death (24). Evidence on management of symptoms is included in [\(cross reference to this paper in series\)](#). Three of the studies (11) (25) (27) included a comparison group. Since the systematic review of this evidence, Da Silva Gane and colleagues have published further evidence reporting quality of life assessments every three months for up to three years in patients with advanced, progressive chronic kidney disease (late stage 4, early stage 5) managed conservatively or by dialysis (15). This is the only longitudinal study which contrasts conservative and dialysis management; conservative patients were older, more dependent and more highly comorbid with poorer physical health and higher anxiety levels than dialysis patients. Their most important finding however was that the conservative patients maintained quality of life, while life satisfaction decreased significantly after dialysis initiation in the dialysis group. Mental health, depression, and life satisfaction scores were overall similar in the two groups at the start of the study. Brown and colleagues have also reported survival, symptom burden, and quality of life in conservatively-managed patients (4), including 273 pre-dialysis patients who had usual nephrology care and 122 non-dialysis pathway patients who also attended a renal supportive care clinic. Median survival in the latter group was 16 (interquartile range, 9, 37) months. With the renal supportive care clinic input, 57% of the non-dialysis patients had stable or improved symptoms over 12 months and 58% had stable or improved QOL.

Although O'Connor and colleagues have proposed that additional head to head studies are needed to compare the symptoms of age-matched dialysis patients, they also felt that the current available studies suggested that quality of life was not significantly different in conservative patients as in dialysis patients (19). The more recent work by Da Silva Gane and colleagues confirms this, and the work by Brown et al suggests that renal supportive care clinics can be effective in controlling symptoms and maintaining quality of life, although the specific interventions need further study.

Beyond physical and psychological symptoms and quality of life, spiritual care needs have also been considered, although critically, in all advanced kidney disease patients rather than specifically in the conservative population. In a prospective cohort study of 253 stage 4 and 5 chronic kidney disease and dialysis patients in Canada, patients reported a mean of 2.9 ± 2.6 spiritual needs, with 69% of patients reporting at least one spiritual need. 32% of patients had high spiritual needs (defined as reporting ≥ 5 of the seven needs). Spiritual needs were associated with age, gender, race, marital status, dialysis modality, time on dialysis, or comorbidity (28). A further study using the same cohort found that adjustment in the domains of psychological distress and extended family relationships appears to mediate some of the beneficial effect of existential well-being on health-related quality of life. Spirituality, however, provides unique variance in patients' quality of life, independent of their psychosocial adjustment (29).

A final piece of important evidence relates to the impact on family of caring for someone with chronic kidney disease stage 5. Work undertaken in the United Kingdom (30) investigated this, and identified confusion about the nature of conservative kidney management. Carers were not aware of the palliative nature of conservative care or the approaching end-of-life issues, and this highlighted some of their unmet support needs. This resonates with evidence directly from patients themselves; that patients' expectations of conservative care are strongly influenced by what is communicated to them by renal staff (31). Even in renal units with established conservative care pathways, there is often only limited information available to patients and families about illness progression and what to expect as the illness progresses.

Conclusion

Evidence on conservative care remains limited. The best evidence is on survival; this does not necessarily reflect what matters most to patients with end-stage kidney disease and their families; instead it reflects what has been studied to date. The published comparative survival outcomes between dialysis and conservative management suffer from inherent methodological flaws which limit any conclusions.

There is no doubt that – in general - dialysis is associated with a significant survival advantage, but this advantage reduces notably for older people with major co-morbidity and poorer functional status. Quality of life, symptoms, and hospital-free survival may be at least as important to consider and actively manage. Before starting kidney replacement therapy, there should be a shared decision-making process based on understanding of prognosis, the potential benefits and harms of therapy, and patient values, goals, and preferences (32). It is not yet known which the best models of care or interventions are for those managed conservatively without dialysis. The limited evidence on cost-effectiveness is summarized in (cross reference to this paper in series), but further study of best ways to improve and maintain quality of life, as well as survival, are needed.

The perspectives on comprehensive conservative care may vary between countries, according to the availability of renal replacement therapy – this is important, and characterizing the different conservative care populations can help. However, there is consensus on how comprehensive conservative care can be defined, and what it includes, and adopting this definition and consistency in what is delivered will help to support service development and future research.

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